DETAILED ACTION

Applicants' arguments, filed 15 April 2010, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Election/Restrictions

Newly submitted claims 32-36 are directed to an invention that lacks a common special technical feature with from the invention originally elected for the following reasons: The special technical features of method claims 32-36 are obtaining various medical images (e.g. ultrasound for claim 32, magnetic resonance for claims 33 and 36, optical image for claim 34, and x-ray image for claim 35). Elected Group I (claims 1-3 and 5-10) is not drawn to obtaining these medical images, and accordingly, does not share a common technical feature with newly added claims 32-36.

Accordingly, claims 32-36 are withdrawn from consideration as lacking unity with the elected invention.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-3 and 5-8 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Kao et al. (Biochimica et Biophysica Acta, Vol. 677, 1981, pp. 453-461) in view of Lanza et al. (Circulation, November 26, 2000, pp. 2842-2847) and Lanza et al. (US 2002/0168320 A1).

In applicant's arguments dated 15 April 2010 (hereafter referred to as applicant's arguments), applicant contends that Kao teaches away from the invention as claimed because Kao teaches that a 24 hour lead time is required for small vesicles to block large vesicle clearance, in contrast to the simultaneous administration required by the instant claims, as of applicant's arguments, page 5, third and fourth paragraph. Applicant quotes Kao, page 457-458 bridging paragraph, which teaches that experiments wherein a blockading dose of small vesicles is has little effect on a blockading dose of large vesicles, as of applicant's arguments, page 5, third full paragraph. Applicant further expresses confusion with regard to the relevance of the Lanza '320 document, as of applicant's arguments, page 6, first full paragraph.

In response, the examiner summarizes what is understood to be the teachings of Kao, along with locations in the Kao reference, as of the table below.

Table I	Simultaneous (1hr) Administration	Blockading Particles administered 24 hours prior to active particles

Active Large Vesicles Blockading Small Vesicles	Case I: Blockade Fails Kao, page 457-458 bridging, Figure 5	Case II: Blockade Succeeds Kao, page 457-458 bridging, Figure 5
Active Large Vesicles Blockading Large Vesicles	Case III: Blockade Succeeds Kao, page 457 Figure 4	Case IV: Blockade Predicted by the skilled artisan to Fail Kao, page 457 Figure 4

In what is described as Case I above, Kao teaches that administration of small blockading vesicles within 4 hours of administration of large active vesicles fails to increase the reticuloendothelial clearance time of the large active vesicles, as of Kao, paragraph bridging pages 457-458 and Figure 5. This failure of reticuloendothelial blockade was pointed out by applicant in applicant's arguments, page 5, third full paragraph. The reason provided by Kao for the failure is that small vesicles naturally have a longer RES clearance time; as such, the large vesicles are cleared before small vesicles have started to accumulate in the RES, as of Kao, page 458 left column. If the small blockading vesicles were administered 24 hours prior to administration of the large active vesicles, the blockading is successful, as of Kao, page 458 Figure 5, and as of applicant's arguments, page 5, as described in Case II of the table above. This is understood to be because both the small vesicles and the large vesicles are present in the RES at the same time, unlike in Case I.

As shown above, Kao's teachings favor a 24 hour difference in administration of the blockading and active particles when the blockading and active particles are of a different size. However, when the blockading and active particles are of the same size, Kao's teachings favor administration that is essentially simultaneous to cause a successful blockade, as further explained by the paragraph below.

As described by Case III of the table below, administration of large blockading particles and large active particles within 1 hour of each other provides an effective blockade, if a sufficient blockading dose is administered. This is evident as of Kao, page 457 left column, Figure 3, reproduced below:

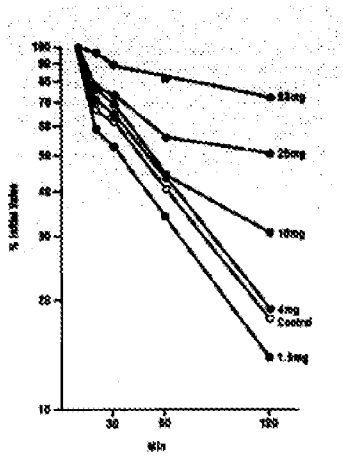

Fig. 3. Blockade of REV clearance by REVs. Rats received a loading dose of unlabelled DPPC/cholesterol REVs via tail vein injection. 1 h later they received a dose of ^{14}C-labelled REVs (4 mg) by the same route. Blood samples were obtained and processed. The points shown represent mean values for three animals.

In the above figure, Kao shows that active large vesicles administered without a blockading dose (i.e. control) were over 80% cleared after about 2 hours (120 minutes). However, when 63 mg of a blockading dose of large vesicles was provided, only about 20% of the active large vesicles were cleared after 2 hours. As such, the skilled artisan would have predicted that administering a blockading and active dose of large particles

that is 24 hours apart would not have reduced RES clearance (Case IV above), because the first dose would have been cleared long before the 24 hour lag between the doses.

As such, it remains the examiner's position that Kao's teachings favor simultaneous administration of the blockading and active doses of particles when both blockading and active doses are essentially of the same size, and have essentially the same RES clearance rate.

The examiner disagrees with applicant's contention that the nanoparticles of the Lanza references correspond to small unilamellar liposomes, as of applicant's arguments, page 5, second paragraphs. While the sizes of said nanoparticles may be indeed be similar to those of small unilamellar liposomes, that does not appear to be the case with regard to their RES clearance rate. As described by Lanza '320, on page 7, last paragraph of the previous office action, the nanoparticles of Lanza comprise avidin-biotin cross-links, which accelerate the RES clearance. As such, the skilled artisan would have expected the particles of Lanza to have been cleared quickly, on a timescale more similar to the quickly cleared large liposomes of Kao as opposed to the slowly cleared small liposomes of Kao. As Kao teaches that administration of the active and blockading doses of large vesicles at essentially the same time successfully provides RES blockade (as of Case III of the table above), simply substituting the quickly cleared particles of Lanza for the quickly cleared large liposomes of Kao is not an unobvious modification. The simple substitution of one known element for another

(the particles of Lanza for the large liposomes of Kao) to obtain predictable results (RES blockade) is prima facie obvious. See MPEP 2143, Exemplary Rationale B.

Claims 9 and 10 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Kao et al. (Biochimica et Biophysica Acta, Vol. 677, 1981, pp. 453-461) in view of Lanza et al. (Circulation, November 26, 200, pp. 2842-2847) and Lanza et al. (US 2002/0168320 A1) as applied to claims 1-8 above, and further in view of Kerr et al. (Expern Opinion on Investigational Drugs, 2000, 9(6), pp. 1271-1279).

In applicant's arguments, page 6, third full paragraph, applicant contends that claims 9 and 10 are patentable for the same reasons as claims 1-3 and 5-8. In response, the examiner points out that claims 1-3 and 5-8 are properly rejected above. As applicant makes no further arguments regarding the limitations of claims 9 and 10, the rejection stands.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ISAAC SHOMER whose telephone number is (571)270-7671. The examiner can normally be reached on 8:00 AM - 5:00 PM Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on (571)272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/I. S./
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612